The “hMRI Toolbox” for quantitative imaging & *in vivo* histology using MRI

#1684

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Highlights

Quantitative magnetic resonance imaging (qMRI) finds increasing application in neuroscience and clinical research due to its greater specificity and its sensitivity to microstructural properties of brain tissue, such as myelin, iron and water concentration. We introduce the **“hMRI Toolbox”**, an easy-to-use open-source tool for generating and processing quantitative MRI data. This toolbox is embedded in the SPM framework, profiting from the high accuracy spatial registration in common space and the variety of available statistical analyses.

It allows the estimation of **quantitative MRI maps**, precisely longitudinal ($R_1=1/T_1$) and effective transverse ($R_2^*=1/T_2^*$) relaxation rates, proton density (PD) and magnetization transfer (MT), followed by spatial registration in common space for statistical analysis. The calculation of other or novel MRI biomarkers of tissue microstructure could be added.

The **hMRI toolbox** can be downloaded from **http://hmri.info**.

The Readme.md and Wiki of the Git repository provide :

- reference documentation, including installation instructions, example dataset, tutorial and detailed description of the functionalities implemented;
- a link to a pre-print paper describing the hMRI toolbox.

Organization of the Toolbox

The toolbox has been developed and tested with MATLAB versions 8.0 (R2012b) to 9.3 (R2017b) and SPM12 versions r6906 and r7219. It is organized in five parts **(Fig.1)**:

Configure Toolbox: A set of standard default processing parameters are provided. The configuration module allows the user to define site- or protocol-specific default parameters to be used across the following processing modules.

DICOM Import: A tool to convert DICOM data into NIfTI files, storing the whole DICOM header as JSON-encoded metadata. By enabling the storage of data acquisition and processing parameters alongside the brain imaging data sets, the hMRI toolbox follows the BIDS recommendations[1].

Auto-Reorient: A simple tool for rigid-body reorientation of all images to the MNI space prior to data processing, in order to ensure the stability of spatial processing steps (mainly segmentation[2]).

Create hMRI Maps (Fig.2): Computes quantitative estimates of R_2^*, R_1, PD and MT from unprocessed multi-echo T_1-, PD- and MT-weighted FLASH acquisitions (stored as NIfTI volumes)[3-6]. The Map creation module corrects the qMRI estimates for spatial receive and transmit field inhomogeneities based on additional reference data[7-9] or using image processing methods[5,10]. Note that there are different methods for PD calculation implemented in the toolbox.

Process hMRI Maps (Fig.3): This module provides dedicated tools and tissue probability maps[11,12] for the spatial processing of the qMRI data based on the SPM spatial processing framework. In particular, spatial registration of the qMRI parameters in standardised space is implemented using the voxel-based quantification (VBQ) approach[11], taking a weighted sum of the qMRI estimates over the spatial extent of the smoothing kernel in native space, and incorporating the Jacobian determinant of the deformation into the weighting (Fig. 3). The weighting is carried out in a tissue-specific manner, producing sets of qMRI maps separately for each tissue class, while reducing partial volume effects on parameter estimates[11].

Figures

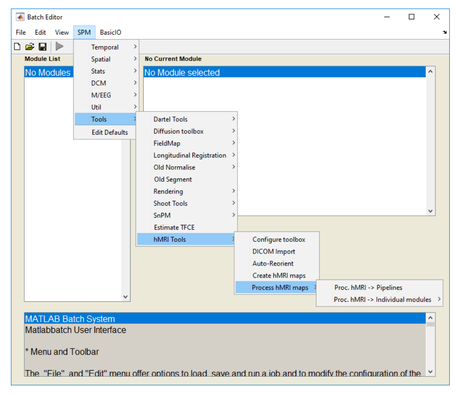

Figure 1 - After installation, the hMRI toolbox can be started from the SPM Batch Editor.
Five choices include
- the configuration of the toolbox,
- DICOM to NIfTI import,
- a reorientation tool,
- the hMRI map creation and
- the spatial processing of the hMRI maps.

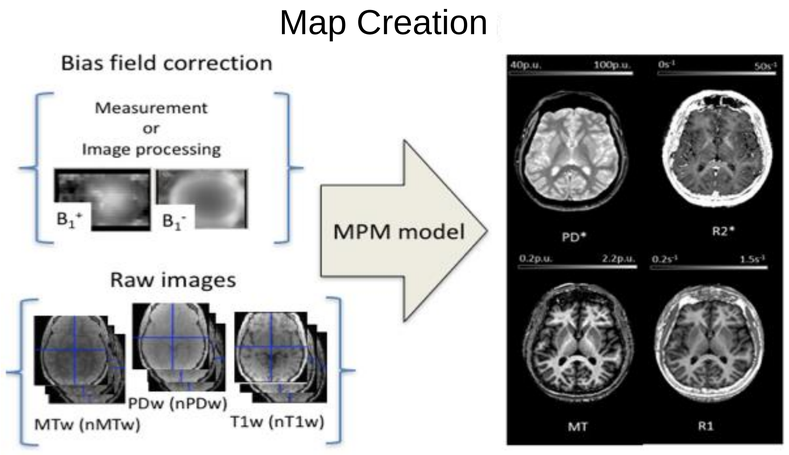

Figure 2 - The MPM protocol includes different multi-echo FLASH scans with predominant T_1-, PD-, and MT-weighting (T_1w, MTw, PDw) by appropriate choice of the repetition time and the flip angle. Optional RF transmit and receive field measurements can be added to the protocol, improving the quality of the MPM maps.
Note that these reference measurements can also be to a limited extent replaced by dedicated image processing steps that are provided by the toolbox. The map creation branch produces maps of proton density (PD), longitudinal relaxation rate (R_1), magnetization transfer saturation (MT) and effective transverse relaxation rate (R_2^*).

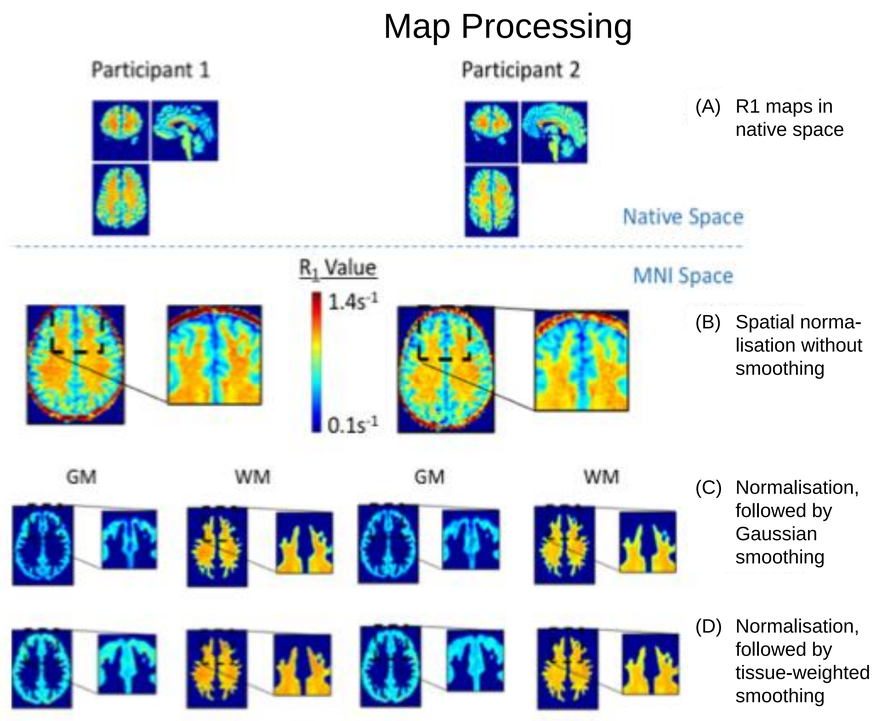

Figure 3 - Spatial registration of qMRI data. Highly parameterised non-linear deformations (e.g. Dartel[22]) allow spatial registration of the qMRI data in standardised space, from (A) to (B). With standard routines, residual inter-individual differences, e.g. in zoomed region in (B) are addressed by spatial smoothing.
However, spatial smoothing leads to bias of the qMRI data, shown in the zoomed region of (C) as a rapid decay in R1 values at tissue boundaries. The voxel-based quantification approach of the hMRI toolbox greatly reduces this smoothing-induced bias (D). Data shown here were acquired at 3T with 800 µm resolution. In all cases the final voxel size of the R1 maps in MNI space was 1mm isotropic resolution. A Gaussian smoothing kernel of 4mm FWHM was used in (C) and (D). This Figure has been adapted from [25] .

Usage of qMRI maps computed with the hMRI Toolbox

The hMRI toolbox provides a time-efficient, robust and simple framework to use qMRI data in clinical and neuroscience research. Quantitative multi-parameter maps (MPM’s) computed with the hMRI toolbox have been used for e.g. (a) the combined study of myelin and iron concentration in brain tissue[13,14], (b) the study of brain atrophy using improved delineation of tissue boundaries[13,15] and (c) assessment of layer-specific microstructure[16] acquiring high-resolution data (800 µm in 25 min. @3T[17], 400 µm in 70 min. @7T[18]). Segmentation of subcortical areas benefits from the multiple, bias-free contrasts of the qMRI data computed by the hMRI toolbox[19,20], leading to improved sensitivity in subcortical regions[21]. The MPM framework is currently used in a multi-site clinical trial (NISCI trial) including different vendors. This has been possible because the MPM acquisition relies mostly on multi-echo FLASH that is available on all modern scanner platforms.
The hMRI toolbox will also allow advanced biophysical modelling of MRI data, such as g-ratio mapping[22,23], for improved inference of brain tissue change at the microscopic level.

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